THE EFFECT OF ADRENALIN ON THE BLOOD PRESSURE OF THE ELASMOBRANCH, SQUALUS ACANTHIAS

LELAND C. WYMAN AND BRENTON R. LUTZ

(*From the Mount Desert Island Biological Laboratory and the Physiological Laboratory of Boston University School of Medicine*)

In elasmobranch fishes the distribution and relative preponderance of the components of the autonomic nervous system and the effects of adrenalin on the heart and digestive tract differ considerably from the same factors in mammals, as pointed out by Lutz (1930*a*, 1930*b*, 1931). The effect of adrenalin (1 : 50,000 to 1 : 25,000) on the heart was found to be inhibitory and was interpreted as the response of an unbalanced parasympathetic mechanism in an organ lacking a sympathetic accelerator innervation (Lutz, 1930*a*). The well-developed chromaphil system seen in elasmobranchs (Lutz and Wyman, 1927) leads one to believe that it must be of functional significance, and a possible inhibitory emergency theory has been suggested to account for its existence (Lutz, 1930*a*). The lack of accelerator nerves to the heart and the failure to demonstrate a vasomotor innervation to the blood vessels makes the abundance of chromaphil tissue in these fishes of especial interest to the physiologist. The well-known effect of adrenalin on the blood pressure of mammals, an effect which is relatively brief and readily duplicated by successive doses, appears to differ from its effect on the blood pressure of cold-blooded animals. Bieter and Scott (1929) reported a rise of blood pressure in the frog following a dose of 0.2 cc. of epinephrine hydrochloride, 1 : 10,000, which persisted for at least one and one-quarter hours after the injection. MacKay (1931) has found that adrenalin causes a rise of ventral aortic blood pressure in skates (*Raia*), which is of much longer duration than the pressor effect in mammals. Herein are reported the results of a preliminary investigation of the effects of adrenalin on the vascular system of the elasmobranch, *Squalus acanthias*. In view of the system of branchial capillaries located between the ventral and dorsal aortæ, simultaneous records of the blood pressures in both systems were considered essential.

Material and Method

Specimens of the dogfish, *Squalus acanthias*, 730 to 1400 grams in weight, taken from Frenchman Bay, Maine, were used. The spinal cord was pithed posteriorly from the level of the sixth vertebra.

The fish was secured in a tank of sea water and the gills were perfused through the mouth as described in a previous paper (Lutz and Wyman, 1931). Simultaneous ventral and dorsal aortic blood pressures were recorded on a smoked drum by means of two mercury manometers and two cannulas, one inserted in one of the first branches of the ventral aorta thus leaving the second, third and fourth holobranchs on that side and all the gills on the other side for respiration, and the other inserted in the coeliac artery close to the dorsal aorta. The cannulas and manometer connections were filled with a physiological solution (urea-saline, Lutz, 1930*a*) containing a little heparin to prevent clotting. Adrenalin chloride (Parke, Davis and Co.), diluted in urea-

TABLE I

Effect of Initial Doses of Adrenalin

Exp. no.	Dose of adrenalin	Increase of pressure Ventral aorta			Increase of pressure Dorsal aorta		Change of heart rate
		Syst.	Diast.	Pulse	Syst.	Diast.	
		per cent	*per cent*	*per cent*	*per cent*	*per cent*	*beats per min.*
30	1 cc. 1 : 1000	71.5	40.0	150.0	75.0	—	−6
31	1 cc. 1 : 1000	29.1	30.8	27.8	53.8	72.8	+4
35	2 cc. 1 : 1000	70.0	46.1	114.1	91.0	80.0	0
36	2 cc. 1 : 1000	55.6	13.3	233.0	—	—	−30
27	2 cc. 1 : 10,000	39.2	38.5	40.0	111.8	133.3	0
29	2 cc. 1 : 10,000	60.0	33.3	100.0	66.5	—	−4
33	2 cc. 1 : 50,000	32.1	20.0	63.6	50.0	50.0	0
34	2 cc. 1 : 100,000	33.3	14.3	60.0	45.5	36.3	−4
37	2 cc. 1 : 500,000	33.3	42.8	23.1	91.6	111.0	+4

saline solution, was injected into the portal vein. MacKay (1931) has shown that in the skate the effects of adrenalin administered in this way are the same as those obtained by injection into a large systemic vein. Control injections of urea-saline solution and adequate controls for manipulation during injections were carried out.

RESULTS

Intravenous injections of adrenalin, in doses of one or two cc. of 1 : 1000 to 1 : 500,000, produced rises of ventral and dorsal aortic blood pressure, both systolic and diastolic, persisting for at least 30 minutes (Table I; Fig. 1, A). No attempt was made to determine the maximum duration of the pressor effect, but MacKay (1931) has found it to be from one to two and one-half hours in the skate. There was also a marked increase of pulse pressure. The effect on the heart rate was not constant, but there was a general tendency

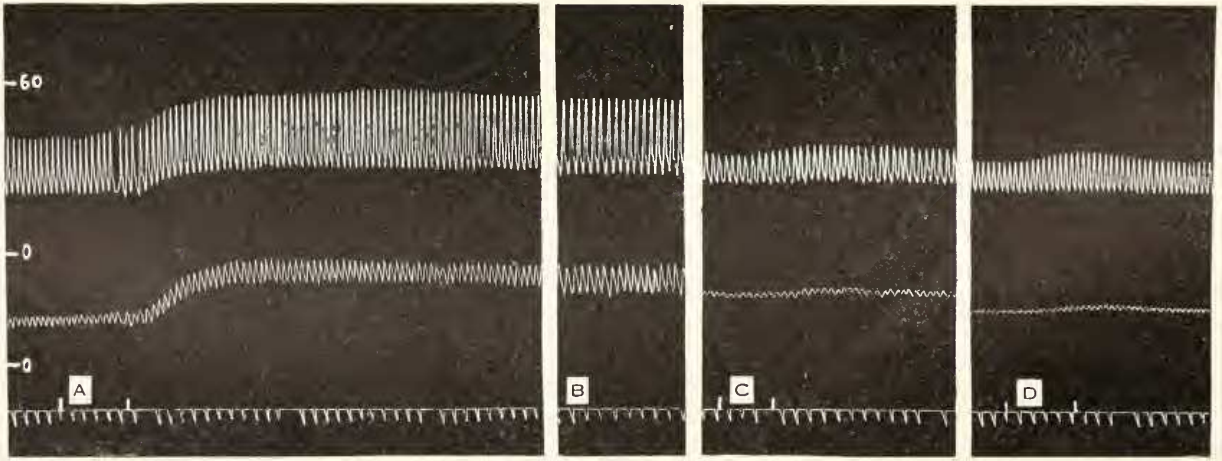

FIG. 1. The effect of adrenalin on the ventral (upper) and dorsal (lower) aortic blood pressures of *Squalus acanthias*. Cord pithed posteriorly from the level of the sixth vertebra. Time record shows five-second intervals. Figures at left show pressure levels in mm. Hg. The zero level (upper) for the ventral aorta is at 40 mm. Hg for the dorsal aorta. A. Exp. 27. Intravenous injection of 2 cc. of adrenalin, 1 : 10,000. B. Blood pressures 32 minutes later. C. Injection of 2 cc. of adrenalin, 1 : 10,000, 41 minutes after the initial injection (A). D. Exp. 33. Control injection of 2 cc. of urea-saline solution.

toward a decrease, especially following the stronger doses (1 : 1000, 1 : 10,000).

Subsequent doses of adrenalin following doses stronger than 1 : 500,000 produced small temporary increases of systolic pressure with little or no effect on the diastolic pressure, and consistent small increases of pulse pressure (Table II; Fig. 1, C). The rise of systolic

TABLE II

Effect of Subsequent Doses of Adrenalin
(For initial doses see Table I)

Exp. no.	Dose of adrenalin	Time after first dose	Increase of pressure Ventral aorta			Increase of pressure Dorsal aorta		Change of heart rate
			Syst.	Diast.	Pulse	Syst.	Diast.	
		min.	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*beats per min.*
27	1 cc. 1 : 1000	33	1.8	11.1	4.3	17.1	16.7	−2
	2 cc. 1 : 10,000	41	2.7	0	8.3	3.8	0	0
	2 cc. 1 : 10,000	51	11.8	4.8	23.0	4.5	0	−2
29	2 cc. 1 : 10,000	7.5	2.6	0	5.9	4.4	—	−6
33	2 cc. 1 : 50,000	10	5.7	16.1	−5.9	15.0	23.5	0
34	2 cc. 1 : 100,000	3.5	3.1	0	6.2	6.2	6.7	+2
	2 cc. 1 : 100,000	8.5	3.1	0	6.2	6.7	0	−4
	2 cc. 1 : 1000	11.5	8.8	6.2	11.1	12.5	13.3	−4
37	2 cc. 1 : 500,000	9.5	20.0	11.1	33.3	33.3	12.5	0
	2 cc. 1 : 500,000	22.5	16.1	12.5	20.0	37.4	33.3	0
	2 cc. 1 : 1000	28.5	12.5	12.5	12.5	41.1	23.1	−6

pressure was, in most cases, actually due to the increase of pulse pressure. The effect of subsequent doses on the heart rate, however, was similar to that of initial doses.

Control injections of 2 cc. of urea-saline solution gave results which were essentially similar to those following subsequent doses of adrenalin with respect to blood pressure and pulse pressure. The heart rate, however, was unaltered (Table III; Fig. 1, D). It is probable, therefore, that such subsequent doses of adrenalin have little or no effect on the blood pressure.

After a dose of two cc. of adrenalin, 1 : 500,000, which gave a less prolonged pressor effect than stronger initial doses, subsequent doses of the same size were effective, producing significant increases of blood pressures and of pulse pressure which again were of shorter duration than the pressor effects of stronger doses (Table II, Exp. 37). This suggests that the ineffectiveness of adrenalin given during the prolonged pressor effect following stronger doses is due to the existence of the maximum pressor action of which the vessels are capable. Such

an explanation obviates the necessity of assuming that a pharmacological tolerance to adrenalin has been acquired.

Excluding cardiac effects, a change in ventral aortic pressure following the administration of adrenalin might be due to alterations in either the gill vessels or in the systemic vessels. The increase of blood pressure following initial doses of adrenalin was often associated with slowing or with no change in heart rate. The percentage increase of diastolic pressure in the dorsal aorta was consistently greater than that in the ventral aorta (Table I). These facts suggest a vasoconstrictor action of adrenalin, peripheral to the gill capillaries. Neither recording the venous outflow from the excised spiral valve (the blood vessels of which were perfused with adrenalin solutions) nor microscopic observation of the minute vessels of the tail, during

TABLE III

Effect of Control Injections of Urea-Saline Solution

Exp. no.	Dose	Increase of pressure Ventral aorta			Increase of pressure Dorsal aorta		Change of heart rate
		Syst.	Diast.	Pulse	Syst.	Diast.	
		per cent	*per cent*	*per cent*	*per cent*	*per cent*	*beats per min.*
31	2 cc.	−3.1	0	−5.2	0	0	0
33	2 cc.	16.7	5.0	40.0	17.6	12.5	0
33	2 cc.	9.6	5.0	18.2	10.5	5.5	0
34	2 cc.	4.2	−12.5	37.5	9.1	—	0
37	2 cc.	11.5	0	23.1	9.1	0	0
37	2 cc.	3.1	0	6.2	5.8	0	0

the injection or direct application of adrenalin, gave evidence of vasoconstriction. Further work is necessary to locate the region of action of adrenalin in producing the pressor effect in *Squalus acanthias.*

There is considerable doubt concerning the existence of a sympathetic vasoconstrictor innervation in elasmobranchs. The long sustained pressor action of small amounts of adrenalin and the accelerator and augmentor action of minute doses on the heart of the skate (Huntsman, 1931) suggest that a possible function of the well-developed chromaffin system is to take the place of sympathetic nervous factors in vascular regulation. However, the discovery by MacKay (1931) of pressor changes in the ventral aorta following sensory stimulation in spinal or anesthetized skates, which were too brief to be due to reflex discharge of adrenin, invites further search for vasoconstrictor nerves.

SUMMARY

1. Intravenous injection of adrenalin, in doses as low as 2 cc. of 1 : 500,000, produced long-sustained pressor effects in *Squalus acanthias*, together with marked increase of pulse pressure and a tendency toward decrease of heart rate.

2. Subsequent doses of adrenalin following doses stronger than 1 : 500,000 were ineffective. This is interpreted as being due to already existing maximum pressor action. Doses subsequent to a dose of 2 cc. of 1 : 500,000 were effective.

3. The pressor effect is interpreted as being due to extra-cardiac factors, peripheral to the gill capillaries, but the region of action of the adrenalin was not located.

BIBLIOGRAPHY

BIETER, R. N., AND F. H. SCOTT, 1929. *Am. Jour. Physiol.*, **91**: 265.
HUNTSMAN, M. E., 1931. *Contr. Can. Biol. and Fish.*, N.S., **7**: 33.
LUTZ, B. R., 1930*a*. *Am. Jour. Physiol.*, **94**: 135.
LUTZ, B. R., 1930*b*. *Biol. Bull.*, **59**: 211.
LUTZ, B. R., 1931. *Biol. Bull.*, **61**: 93.
LUTZ, B. R., AND L. C. WYMAN, 1927. *Jour. Exper. Zoöl.*, **47**: 295.
LUTZ, B. R., AND L. C. WYMAN, 1931. *Biol. Bull.*, **61**: 217.
MACKAY, M. E., 1931. *Contr. Can. Biol. and Fish.*, N.S., **7**: 19.